Dear Physicians,

In this issue of the Ochsner Cancer Institute’s “Outcomes in Oncology” newsletter, Dr. Brian Moore, the Division Head of Head and Neck Cancer at Ochsner describes important clinical innovations in the management of oropharyngeal cancer inspired by a changing epidemiology of the disease and new multimodality treatment concepts. These treatment approaches have resulted in less morbid outcomes for the patient suffering from this cancer without detriment in the ability to cure the disease.

Focused, lower dose radiation therapy combined with targeted chemotherapy and new minimally invasive, robotic surgical approaches for removing the tumor are important advances in the care of the patient with oropharyngeal cancer. The Head and Neck Oncology team at Ochsner are leading the region in the use of these exciting treatment opportunities.

The Ochsner team’s focus on treating the “entire patient”, including their physiological and emotional needs during their cancer therapy is also clearly projected by Dr. Moore in this account of the multidisciplinary management of their patients with oropharyngeal cancer.

As our stated mission, the purpose of the “Outcomes in Oncology” newsletter series is to provide health care professionals of the Gulf South with timely and accurate accounts of important cancer problems that they may encounter in their daily practices. Thank you for participating in this important educational effort provided by the Ochsner Cancer Institute.

Sincerely,

Rodney J. Landreneau, M.D.
Medical Director, Ochsner Cancer Institute

Head and Neck Cancer Update: New Strategies for the Treatment of Oropharyngeal Cancer

---

Head and Neck Cancer Team:

Head and Neck Surgical Oncology:
Brian A. Moore, MD, FACS
Christian P. Hasney, MD

Radiation Oncology:
Troy Scroggins, MD
Mini ElNaggar, MD
Roland Hawkins, MD

Medical Oncology:
Suma Satti, MD
Marc Matrana, MD
Chris Theodossiou, MD

Speech-Language Pathology:
Charlotte Ducote, PhD
Yvette Peevy, MA, CCC-SLP
Leah Legere, MA, CCC-SLP

Psycho-Social Oncology:
Joel Marcus, PsyD
Clinical Update on Oropharyngeal Cancer

Head and neck cancer constitutes a heterogeneous group of malignancies affecting the upper aerodigestive tract, the salivary glands, the thyroid and parathyroid glands, and the skin with varying treatments based upon tumor biology and tumor locations associated with important organ function (i.e., larynx, skull base).

The emergence of human papillomavirus (HPV)-associated oropharyngeal squamous cell carcinoma (OPSCC) has sparked renewed debate and research focus into the optimal treatment of this particular form of head and neck cancer. Novel treatment approaches for oropharyngeal carcinoma (anatomically, the soft palate, palatine tonsils, lateral and posterior pharyngeal walls, and the tongue base) aim at reducing the morbidity of chemoradiation therapy and surgery through the incorporation of minimally invasive surgery and “deintensification” strategies with newer chemotherapy agents and altered radiation therapy fractionation schemes.

In this issue of “Outcomes in Oncology” these exciting new approaches to the changing nature of oropharyngeal carcinoma will be described.

HPV-Associated Oropharyngeal Squamous Cell Carcinoma

Carcinoma of the oral cavity and pharynx is the eighth most common cancer in men, with an estimated incidence between 2005-2009 of 16.4/100,000 in the United States. Although less common in females, the incidence of oropharyngeal cancer is on the rise, with the majority of these new cases attributed to antecedent HPV infection, particularly with HPV-16, and involving the palatine or lingual tonsils (tongue base) (1,2).

Conversely, the incidence of SCC in other head and neck mucosal subsites such as the larynx and hypopharynx has been declining, potentially attributable to decreases in smoking rates (1).

Historically, patients who developed OPSCC were older males with extensive histories of smoking and alcohol use. Patients with HPV-associated OPSCC are typically younger, with less alcohol and tobacco exposure than traditional OPSCC patients. They present with poorly differentiated or basaloid tumors and advanced stage disease, usually due to significant cervical lymph node metastases (3). Oral HPV-16 infection, seropositivity to HPV-16 L1 capsid protein and prior oral infection with any HPV subtype are associated with the development of HPV-associated OPSCC (4).

The rise in the incidence of HPV-related OPSCC has been attributed to changing sexual habits. Oropharyngeal cancer has been linked to a rising number of vaginal-sex partners and a high lifetime number of oral sex partners (2). The diagnosis of HPV-related OPSCC can be accomplished with immunohistochemistry staining of needle aspirates or tissue for p16 overexpression, as well as detection of HPV DNA through a variety of methods (3).

Across these various studies, patients with HPV-related OPSCC have demonstrated significantly improved outcomes, with better survival and disease control, as well as decreased rates of second primary tumors, compared to HPV-negative tumors (6). HPV status is not entirely protective against the deleterious effects of smoking, as the number of pack-years smoked and years smoking, both prior to diagnosis and during treatment, have been shown to increase the risk of OPSCC progression and death, even in HPV-related OPSCC (7).

Evolving Treatment Paradigms

The rapid evolution of minimally invasive surgical approaches to the head and neck, targeted molecular therapy and 3-D conformal radiation therapy has led to increasing specialization and regionalization of head and neck cancer care, with a focus on creating dynamic multidisciplinary teams to address all facets of a patient’s diagnosis, treatment, rehabilitation, and survivorship.

This team approach defines head and neck cancer care at the Ochsner Cancer Institute. Patients are evaluated by a multidisciplinary team that includes fellowship-trained head and neck surgical oncologists/reconstructive microsurgeons, radiation oncologists, medical oncologists, speech and language pathologists, and a psychosocial oncologist, among others.

Such multidisciplinary head and neck cancer care has demonstrated improved adherence to published guidelines, shorter times to start therapy, decreased length of stay and even improved survival in patients with stage 4 cancer (4,5).

Many patients with OPSCC, regardless of HPV status, present with advanced (stage 3 or 4) disease. The majority historically receive radiation therapy, often with concurrent chemotherapy (either cisplatin or cetuximab); although, various strategies for induction chemotherapy have been investigated.

Brian Moore, M.D.
Despite the improved outcomes and decreased risk of death with HPV-related OPSCC, traditional radiation therapy with or without chemotherapy has been associated with significant post-treatment dysphagia, often with feeding tube dependence and decreased quality of life. The treatment side effects following such organ preservation approaches persist years after therapy and can be profound, including dysarthria, dysphagia, trismus, cranial neuropathies and even osteoradionecrosis (8).

Early intervention by speech and language pathology, continued oral intake throughout radiation and active execution of swallowing exercises have been shown to decrease swallowing dysfunction following nonsurgical treatment of OPSCC (9).

The improved outcomes of patients with HPV-related OPSCC and the frequent deleterious long-term effects of chemoradiation therapy triggered investigation into strategies to deintensify treatment for OPSCC. Alterations in chemotherapy agents used as radiation sensitizers, incorporation of induction chemotherapy into a sequential approach to radiation therapy, decreases in radiation dose and up-front transoral surgery are all targets for ongoing multi-institutional studies (10).

Radiation Therapy Oncology Group (RTOG) 1016 is an open, multi-institutional trial investigating cetuximab with accelerated fractionation radiation versus cisplatin with the same radiation treatment protocol. As a participating institution in the RTOG, as well as the Eastern Cooperative Oncology Group (ECOG) and the Alliance for Clinical Trials in Oncology, Ochsner is actively accruing patients for this trial.

Technological innovations now enable surgeons to perform transoral resection of oropharyngeal tumors with neck dissection followed by adjuvant therapy as indicated. Both transoral laser microsurgery and TransOral Robotic Surgery (TORS) for oropharyngeal tumors have revolutionized surgical therapy with the potential to achieve comprehensive resections without the morbidity of traditional approaches that require facial incisions, mandibulotomy or reconstruction (11).

By facilitating high-resolution, three-dimensional visualization and precise, scaled surgical motion without the morbidity of the traditional lip- or mandibular-splitting approaches required for access to the oropharynx, TORS has emerged as a feasible and safe technique to remove T1 and T2 lesions of the tonsil and tongue base, benefiting numerous patients at Ochsner Cancer Institute (OCI) over the past two years (Figures 1-4) (11).

Based on the success of minimally invasive surgical approaches and the apparent favorable side effect profile, transoral surgery for oropharyngeal SCC is now being evaluated against chemoradiation therapy in two multi-institutional trials: RTOG 1221 in patients with HPV-negative oropharyngeal cancer and ECOG E3311 in patients with HPV-related OPSCC.

As the incidence of HPV-related OPSCC continues to rise, information gleaned from these ongoing research endeavors has the potential to improve not only disease control but also functional outcomes for patients with head and neck cancer.

**Psychosocial Support and Head and Neck Cancer**

Care for the patient with head and neck cancer does not stop with treatment of the tumor itself. Depression and distress are commonly encountered in head and neck cancer patients, and these challenges must also be addressed by the Multidisciplinary Head and Neck Team (12). Failure to adequately address these issues has been shown to contribute to reduced survival in head and neck cancer patients (13).

Thankfully, early identification of distress and early referral to psychotherapy has been shown to decrease rates of post-traumatic stress disorder, anxiety and depression (12). Similarly, early (or even prophylactic) treatment with escitalopram has been shown to decrease the rate of developing depression by more than 50 percent, with attendant improvements in quality of life as well (13).

Due to the impact of early identification and intervention to combat the depression and distress that typically accompany diagnosis and therapy for head and neck cancer, psychosocial support services are integral to true multidisciplinary care.

**Multidisciplinary Care**

The rising rate of HPV-related OPSCC is leading to an emerging epidemic in which more patients will potentially suffer from head and neck cancer than ever before. Advances in minimally invasive surgery, reconstruction, radiation therapy and chemotherapy, including targeted molecular therapy, are continually emerging to treat the disease. However, the morbidity of head and neck cancer is often extensive, adversely affecting fundamental human actions such as speech and swallowing, as well as patients’ mental health.

To meet these multifaceted challenges, a true multidisciplinary team is required to effectively treat these patients, not only giving them the best chance of cure, but also functional recovery. This defines the Ochsner approach, which is reflected in the improved outcomes of patients with pharyngeal cancer treated at our institution, compared to national averages (Figure 5). Currently open, actively-enrolling multidisciplinary protocols available for head and neck cancer at OCI are listed in Table 1.
Figure 1. Contrasted computed tomography (CT) scan of the neck in a 53-year-old male who presented with a left neck mass, initially thought to represent an unknown primary SCC, based on fine needle aspiration biopsy.

Figure 2. Transoral robotic surgery (TORS) view of a T1 SCC of the left tonsil. The arrow denotes the tumor that was hidden from clinical view by a prominent anterior tonsillar pillar. The posterior pharyngeal wall is marked with a (+) sign, and the tongue base is indicated by the star. The patient underwent a TORS lateral oropharyngectomy with negative margins and a modified neck dissection, revealing T1N1M0 SCC of the tonsil with no adverse features. Radiation therapy was not recommended based on favorable pathologic data.

Figure 3. The head and neck surgeon is able to comprehensively excise tumors from the oropharynx using the surgical robot.

Figure 4. Typical operating room setup for TORS. The endoscope and operating arms of the robot are inserted through the mouth, and a bedside surgeon assists the operating surgeon who is seated at the console as above.

Figure 5. Ochsner Cancer Institute survival data for cancer of the pharynx, by stage, based on Cancer Registry data, 2003-2012.
Continuing Medical Education Questions

1. The majority of new cases of oropharyngeal squamous cell carcinoma have been attributed to
   a. Smoking/tobacco use
   b. Alcohol consumption
   c. Human papillomavirus (HPV) infection
   d. Synergistic effects of tobacco and alcohol

2. The clinical features of HPV-associated oropharyngeal cancer include all of the following except:
   a. Younger age at presentation (versus HPV-negative tumors)
   b. Poorly differentiated or basaloid histology
   c. Rare cervical lymph node metastases
   d. Advanced stage at presentation due to lymph node metastases

3. Early psychosocial intervention as part of a multidisciplinary approach to head and neck cancer has been shown to decrease all of the following except:
   a. Post-traumatic stress disorder
   b. Distress
   c. Quality of life
   d. Depression

Upcoming CME Oncology Activities:

- May 20, 2014
  11th Annual Research Day
  Brent House Atrium, New Orleans, LA

- June 5-8, 2014
  12th Annual New Orleans Aeroallergen Conference
  Brent House Conference Center, New Orleans, LA

- June 12-15, 2014
  Gulf States Hospital Society Conference
  Grand Marriott, Point Clear, AL

- June 27, 2014
  Pulmonary Hypertension Conference
  Brent House Conference Center, New Orleans, LA

Information and registration for all conferences are available on our website at ochsner.org/cme

Accreditation

The Ochsner Clinic Foundation is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians.

Designation

The Ochsner Clinic Foundation designates this enduring material for a maximum of 1 AMA PRA Category 1 Credits™. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

For answers to questions, see below.

References


Table 1. Open Intergroup Clinical Trials at Ochsner Cancer Institute

| RTOG 1016 | Phase III Trial of Radiotherapy Plus Cetuximab Versus Chemoradiotherapy in HPV-Associated Oropharynx Cancer |
| RTOG 1216 | Randomized Phase II/III Trial of Surgery and Postoperative Radiation Delivered with Concurrent Cisplatin versus Docetaxel versus Docetaxel and Cetuximab for High-Risk Squamous Cell Cancer of the Head and Neck |
Important Thoracic Cancer Treatment Protocols at Ochsner Cancer Institute

Table 1. Open Intergroup Clinical Trials at Ochsner Cancer Institute

<table>
<thead>
<tr>
<th>Trial</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>RTOG 1016</td>
<td>Phase III Trial of Radiotherapy Plus Cetuximab Versus Chemoradiotherapy in HPV-Associated Oropharynx Cancer</td>
</tr>
<tr>
<td>RTOG 1216</td>
<td>Randomized Phase II/III Trial of Surgery and Postoperative Radiation Delivered with Concurrent Cisplatin versus Docetaxel versus Docetaxel and Cetuximab for High-Risk Squamous Cell Cancer of the Head and Neck</td>
</tr>
</tbody>
</table>

For more information regarding these and other clinical trials active at Ochsner Cancer Institute, visit our website, ochsner.org/ochsner_cancer_institute, or contact Ochsner Protocol Office Director, Kimberly Henry at 504-842-0275.

Upcoming “Outcomes in Oncology” Topics:

**June:** Urologic Oncology
**July:** Dermatologic Oncology
**August:** Colorectal Oncology
**September:** Hepatobiliary Malignancy
**October:** Breast Cancer
**November:** Gynecologic Oncology
**December:** Neurooncology

To refer a patient to our Head and Neck Surgical Oncology Clinic, please call Lead Nurse Daphne Black at 504-842-4080. For 24/7 phone consults and/or patient transfers, please call the Regional Referral Center at 1-855-OHS-LINK (647-5465).